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Haemodynamic response during initiation of non-invasive positive pressure ventilation in COPD patients with acute ventilatory failure

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The aim of this study was to check non-invasively the acute haemodynamic effects of non-invasive positive pressure ventilation (NPPV) initiation in patients with chronic obstructive pulmonary disease (COPD) and acute ventilatory failure (AVF). Nineteen consecutive COPD patients with AVF were evaluated clinically and echocardiographically during spontaneous breathing with O_2 supplementation and during NPPV plus O_2. NPPV was administered with a scheduled inspiratory pressure of 15 cmH_2O and an expiratory pressure of 4 cmH_2O, via facial mask. Arterial blood gas improved significantly (pH and $PaCO_2$; $P<0{\cdot}001$) during NPPV administration in all patients; none had hypotension or acute arrhythmia. Doppler echocardiographic evaluation was feasible in most of the patients (16/18). With reference to baseline values, no significant changes in pulmonary artery pressures and cardiac output (CO) were observed by Doppler echocardiography in most patients. Only four patients (21%) showed a significant reduction (>15%) of CO during NPPV. No correlation was found between decreased CO and baseline data, but three patients showing CO reduction had poor tolerance to mask ventilation and did not improve respiratory rate during NPPV. It was concluded that the initiation of NPPV by facial mask does not alter haemodynamics acutely in most COPD patients with AVF, but individual patients may experience reduction in CO in spite of adequate oxygen saturation levels. This suggests that caution should be used when applying pre-determined and fixed pressures during NPPV. Monitoring haemodynamics by Doppler echocardiography may be useful for early detection of haemodynamic alterations due to NPPV application in patients with AVF.

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Introduction

Recent, prospective, randomized trials (1–3) have clearly established non-invasive positive pressure ventilation (NPPV) by nasal or facial mask as a first-line treatment in selected patients with acute ventilatory failure (AVF) due to exacerbation of chronic obstructive pulmonary disease (COPD). In the last few years, a number of controlled and uncontrolled studies, involving more than 500 patients, have appeared in the literature (4), demonstrating very low complication rates associated with NPPV. Moreover, no report exists to date on NPPV-related haemodynamic complications in COPD patients with AVF in the literature, Conversely, it is well known that invasive mechanical ventilation may seriously alter haemodynamic status by decreasing cardiac output and modifying blood flow distribution (5). The intubation and initiation of positive pressure ventilation in acute exacerbation of COPD (6) is one of the clinical settings which is most likely to trigger haemodynamic compromise. In theory, relatively low support pressures, together with the absence of neuromuscular blockade and sedation, should produce a lower impact of NPPV on haemodynamics. The aim of this study is to assess whether or not the initiation of NPPV by face mask with scheduled inspiratory and expiratory positive pressures can acutely modify haemodynamic status in COPD patients with AVF. For this purpose, we used colour Doppler echocardiography, a non-invasive technique suitable for haemodynamics evaluation in ventilated and COPD patients (7–9).

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Methods

SUBJECTS

We studied 19 COPD patients (14 males and five females, mean age 67 ± 9 years) who were admitted for management

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of decompensated AVF. COPD diagnosis was confirmed by patient history and physical examination as well as by previous pulmonary function tests. Patients were considered eligible for the study if they conformed with the following criteria:

- respiratory acidosis and AVF (at least two of the following blood gas values: pH <7·30, $PaCO_2$ >7·90 kPa, PaO_2 <7·98 kPa) due to exacerbation of COPD;
- absence of coma;
- absence of haemodynamic instability (uncontrolled cardiac arrhythmias and/or systolic blood pressure <90 mmHg).

An illness-severity score, simplified acute physiologic score (SAPS) (10), and a neurological score, specifically designed for respiratory patients by Kelly and Matthay (11), were determined for each patient at study entry.

PROTOCOL

At hospital admission, each patient received oxygen supplementation and aerosolized salbutamol (1·25 mg) and ipatropium bromide (0·25 mg) plus beclomethasone (40 mg) in an emergency room setting. After 15–20 min, patients were transferred to the respiratory intermediate intensive care unit (RIICU), for NPPV plus O_2 therapy. Patients received O_2 therapy alone for almost 30 min altogether. NPPV was begun with O_2 supplementation adjusted to give an arterial O_2 saturation of 90–92%. Patients were sequentially evaluated clinically (including non-invasive blood pressure) and echocardiographically during O_2 supplementation at RIICU admission (after 30 min of oxygen supplementation) and during NPPV plus O_2 after a 30 min lapse. Randomization of treatment order was not performed since (a) emergency room, acute respiratory distress patients routinely receive oxygen supplementation before a medical visit, (b) no acute haemodynamic changes in exacerbated COPD and acute respiratory failure patients treated with oxygen supplementation have been reported to date (12–14) and lastly (c) we wished to avoid the hysteretic effect caused by positive pressure ventilation (15). Particular care in patient timing management was performed to guarantee from the lack of random order in NPPV application (16). Also, echocardiograph personnel were not aware of the background or aim of the study at the time of Doppler measurements. Furthermore, ethical concerns prohibited baseline evaluation of patients breathing without oxygen supplementation and the inclusion of a non-ventilated control group. Informed consent was given by the patients or next of kin. The study was approved by the Local Ethics Committee.

NON-INVASIVE VENTILATION

NPPV was delivered by a bi-level positive airway pressure (BiPAP® S/T-D, Respironics Inc, Murrisville, PA, U.S.A.) through a facial mask (Gibeck Respiration AB, Upplands-Väsby, Sweden). BiPAP (17 is a flow-triggered device working as a pressure support (PSV) which can apply external positive end-expiratory pressure (PEEP). We applied BiPAP in spontaneous mode with a scheduled inspiratory pressure support of 15cmH_2O and an expiratory positive pressure of 4 cmH_2O. We chose these pressure levels based on our clinical experiences of NPPV efficacy (18,19) and on the reported experiences of other authors (20–23). A pneumologist assisted to facilitate patient co-operation at all times. The mask cushion was inflated with about 20 ml of air for perfect adherence to the patient's face and particular care was taken to avoid possible air leaks. Before and during NPPV application, oxygen was administered at the lowest flow to provide an arterial oxygen saturation of 90–92% under oxymetric control (Pulsox 7, Minolta, Avl AG, Switzerland). Patient compliance with ventilation was evaluated by the physician in charge.

ECHOCARDIOGRAPHIC MEASUREMENTS

Two-dimensional, continuous wave (CW), pulsed-wave and colour Doppler echocardiography (Hewlett-Packard 77020A, ultrasound imaging system, Andover, MA, U.S.A.) was performed using 2·5 MHz imaging transducers. Doppler recordings of tricuspid regurgitation velocity and pulmonary flow were attempted from parasternal, apical and subcostal approaches. The 'contrast-enhancement' technique (agitated isotonic saline i.v. injections) was used in selected patients to increase the quality of CW Doppler tracings (24). Maximum velocity of tricuspid regurgitation jet (TR) was measured by CW Doppler imaging. The simplified Bernoulli equation was used to calculate the systolic transtricuspid gradient which was added to mean right atrial pressure (clinically estimated) to predict pulmonary artery systolic pressure (PASP), according to a validated technique (25). The pulsed Doppler technique was used to study pulmonary artery systolic flow velocity, as described by Kitabatake *et al.* (26). Acceleration time (AcT) was defined as the interval between the onset of ejection and peak flow velocity. Right ventricular ejection fraction time (RVET) was defined as the interval between ejection onset to zero flow velocity. We also used the regression equation proposed by Mahan *et al.* (27), which involves AcT, to predict pulmonary artery mean pressure (PAMP).

Blood flow velocity through the aortic valve was assessed by pulsed Doppler echocardiography using a suprasternal approach. Cardiac output (CO) was calculated as the product of the cross-sectional area of the aorta, aortic flow velocity integral and heart rate. Cardiac index (CI) was derived by dividing CO by body surface area. This standard method was extensively validated and used also in COPD patients (28–30). Two-dimensional echocardiographic data, as such the end-diastolic right ventricular:left ventricular dimensions ratio (RVEDD:LVEDD), even though they are useful in a clinical setting (31), were not considered because they are not validated and difficult to obtain in hyperinflated patients.

Since the spontaneous variability of pulmonary artery pressure in COPD patients at rest has a coefficient of

TABLE 1. Patients' characteristics at hospital admission

Patient no.	Age (years)	Sex	Mean BP (mmHg)	PaO_2 (kPa)	$PaCO_2$ (kPa)	pH	Oedema of the legs	RR (breaths min^{-1})	HR (beats min^{-1})	Kelly score*	SAPS	Baseline† FEV_1/FVC (%)
1	72	M	133	5·18	11·7	7·28	=	28	88	2	13	40
2	64	M	106	7·18	7·84	7·35	=	26	96	1	6	31
3	73	M	83	4·78	10·26	7·29	+++	32	102	3	18	48
4	64	M	97	6·46	9·56	7·34	+	28	75	1	8	38
5	51	F	102	5·98	11·71	7·17	=	30	118	2	12	36
6	78	M	110	4·65	10·1	7·19	++	30	120	3	16	?
7	59	M	170	4·89	10·2	7·28	+++	38	90	2	17	29
8	75	M	111	7·71	9·5	7·17	?	36	120	2	14	35
9	58	M	100	4·65	13·73	6·99	+	40	122	3	13	37
10	73	M	103	4·42	13·75	7·15	=	48	99	2	11	36
11	78	M	113	6·38	11·67	7·22	=	34	110	2	15	33
12	72	M	123	6·38	9·84	7·31	+++	32	115	2	17	30
13	67	F	150	4·78	7·71	7·25	=	32	108	1	11	46
14	85	F	93	5·85	11·17	7·19	=	12	130	3	10	?
15	72	F	93	5·18	9·94	7·32	+	28	100	3	9	45
16	56	M	106	6·25	9·27	7·27	=	27	96	1	4	34
17	72	M	93	6·11	9·94	7·32	++	30	100	1	5	40
18	65	F	93	5·18	9·84	7·29	=	30	90	2	8	33
19	54	M	85	6·51	8·15	7·33	=	22	100	1	6	38
Mean	67·7	=	108·6	5·7	10·25	7·25	=	30·6	100·1	2	11·2	37
SD	9·14	=	22·11	0·9	1·76	0·09	=	7·3	14·09	0·8	4·3	5·49
SE	2·1	=	5·07	0·2	0·38	0·02	=	1·6	3·23	0·2	0·9	1·33

*Neurological score by Kelly and Matthay to assess neurological status in patients with acute respiratory failure (11).
†The latest available data before hospital admission.

variation up to 10–6% (32) and since cardiac output measured by echocardiography shows a variability up to 12% (33), we decided that echo Doppler parameter variations of 15% or more would be considered significantly relevant.

REPEATABILITY OF ECHOCARDIOGRAPHIC MEASUREMENTS

Doppler echocardiography was performed by two trained cardiologists from two different institutions. Validation of echocardiograph measurements was previously described by others with regard to CO and PAP (25,30). Repeatability of the technique by the two observers, blinded to each other's results, was previously carried out for eight subjects (four COPD and four healthy subjects; five males; mean age 61<8 years) according to the methodology proposed by Bland and Altman (34).

STATISTICAL ANALYSIS

Individual data and mean ± SD and SE are presented in the tables. Since the data conform with a normal distribution, statistical analysis for values obtained before and during NPPV were performed by paired Student's t testing with Bonferonni's adjustment. A linear regression analysis was used to search for a correlation between haemodynamic and respiratory–clinical data. Statistical significance was defined as $P<0·05$.

Results

Baseline characteristics of patients at admission are shown in Table 1. Study population showed, as a whole, pulmonary hypertension and a mild increase of CO. Heart rate ($P=0·265$), systolic and mean systemic blood pressures (respectively $P=0·054$ and $P=0·134$), systolic PAP ($P=0·063$), mean PAP ($P=0·298$), cardiac output ($P=0·829$) and cardiac index ($P=0·851$) did not change significantly during the application of BiPAP through a face mask in the study population considered as a whole. After 30 min of NPPV application, no significant changes were observed in PaO_2 values when compared with PaO_2 following oxygen therapy alone. On the contrary, significant differences were found between pH, $PaCO_2$ and RR assessed during O_2 therapy alone and during NPPV (Table 2). Table 2 shows the results of echocardiograph evaluations (mean ± SD). Most of the 19 acute COPD patients did not have significant changes in Doppler findings, while six (31·5%) showed variations ≥15% of Doppler haemodynamic parameters during NPPV plus O_2 when compared with O_2 therapy alone. Four of these patients experienced

TABLE 2. Patients' measurements during O_2 supplementation and after 30 min of NPPV (mean ± SD)

Parameters	O_2 alone	O_2+NPPV	*P* value
pH	7·25 ± 0·09	7·32 ± 0·05	<0·001*
PaO_2 (kPa)	8·71 ± 1·11	8·75 ± 1·01	0·870
$PaCO_2$ (kPa)	10·25 ± 1·76	8·57 ± 1·09	<0·001*
RR (breaths min^{-1})	30 ± 7	25 ± 3	<0·001*
Mean BP (mmHg)	109·58 ± 21·97	104·68 ± 13·45	0·134
Systolic BP (mmHg)	150·25 ± 31·27	141·50 ± 19·74	0·064
HR (beats min^{-1})	100·42 ± 16·09	97·84 ± 16·35	0·265
PAMP (mmHg)	37·27 ± 5·38	35·63 ± 5·30	0·298
AcT/RVET	0·38 ± 0·04	0·40 ± 0·06	0·089
PASP (mmHg)	59·27 ± 13·83	55·89 ± 13·26	0·063
CO (l min^{-1})	6·59 ± 1·93	6·65 ± 2·03	0·829
CI (l min^{-1} m^{-2})	3·53 ± 0·86	3·56 ± 0·97	0·851

*Statistically significant.

TABLE 3. Patients showing changes of ≥15% in echocardiographic haemodynamic measurements after 30 min of NPPV administration plus O_2

Patient no.	PASP (mmHg)	PAMP (mmHg)	CI (l min^{-1} kg^{-1} m^{-2})	Systolic BP (mmHg)	Diastolic BP (mmHg)	HR (beats min^{-1})	RR (breaths min^{-1})	Mask tolerance	$PaCO_2$ (kPa)	pH
3 O_2	82	47·5	2·85	110	70	102	32		10·26	7·29
3 O_2+NPPV	82	45	2·25 (−21%)	115	85	100	34	Poor	8·24	7·35
5 O_2	NA	43	4·5	145	80	119	30		11·91	7·17
5 O_2+NPPV	NA	34 (−21%)	3·5 (−22%)	140	80	113	26	Good	7·84	7·33
6 O_2	78	43	4·55	150	90	86	30		10·1	7·19
6 O_2+NPPV	66 (−16%)	39	5·76 (+26%)	150	90	110	28	Good	8·67	7·29
10 O_2	NA	32	4·3	150	80	99	48		13·73	7·15
10 O_2+NPPV	NA	25 (−22%)	3·57 (−17%)	160	90	91	36	Poor	10·46	7·25
11 O_2	60·4	43	2·39	160	90	110	34		11·67	7·22
11 O_2+NPPV	61	43	3·2 (+33%)	140	80	82	26	Good	8·28	7·34
14 O_2	45	NA	4·23	130	80	125	28		11·1	7·29
14 O_2+NPPV	37·3 (−18%)	NA	3·63 (−15%)	140	80	108	32	Poor	9·17	7·34

NA, not assessed.

consistent decreases in cardiac output, although cardiac output increased for the remaining two. Moreover, four patients showed a significant reduction of PASP and/or PAMP. Table 3 shows data for patients who had PAP and/or CI changes ≥15% during NPPV. No correlation was found between decreased CO and baseline data. Conversely, three patients showing CO reduction had poor tolerance to mask ventilation and did not improve RR during NPPV. All the remaining patients showed good compliance with mask ventilation. All but two patients (17/19) had a successful outcome with NPPV therapy (success rate 89·5%).

REPEATABILITY AND FEASIBILITY OF DOPPLER MEASUREMENTS

Both intraobserver and interobserver variability for PASP, PAMP and CI was less than 6%. One or more haemodynamic parameters were obtained by Doppler

echocardiography in most of the patients (16/18=89·5% of the study population). Tricuspid regurgitation was detected in 57%, though Doppler recording quality was adequate for velocity measurements in 47%. Pulmonary flow velocity profiles were obtained from 12 of the 19 COPD patients (63%). Also, tracings of these 12 patients sufficed for mPAP evaluation. Determination of cardiac output was possible in 89% of subjects.

Discussion

Initiation of invasive mechanical ventilation by endotracheal intubation may cause alteration of haemodynamics, especially in patients with AVF, because of acute exacerbation of COPD (6,36). In this clinical setting, a reduction in systemic venous return, the administration of sedative drugs before intubation and the effects of progressive hyperinflation–auto-PEEP and fluid depletion are considered to be the major contributors to hypotension (5,6,37,38). Recently, NPPV has been introduced as an alternative to endotracheal intubation in severe exacerbation of COPD (39,40). Although NPPV is widely used for patients with COPD and AVF, no mention of negative haemodynamic effects of NPPV appears in the English language literature (4,41).

In the present study, we show that, during the initiation of NPPV, some haemodynamic alteration may take place in individual COPD patients with AVF, In fact, four patients (21%) showed reduction of cardiac index during NPPV. It is worth noting that no patients had hypotension during NPPV administration. Indeed, NPPV application did not significantly change haemodynamics in most of our study population and, after 30 min of NPPV, the main haemodynamic data (cardiac output and cardiac index, pulmonary and systemic blood pressures) remained stable in 13 patients (68·4%). Moreover, arterial pH and $PaCO_2$ improved significantly during NPPV administration in all patients.

The maintenance of normal CO after 30 min of NPPV in the majority of the patients was not due to an increase in heart rate, as this remained stable or decreased. Also, in patients showing decreases of CO during NPPV, no correlation was found with baseline data. Nevertheless, three of these patients showed a poor tolerance to mask ventilation, as was, also confirmed by stable or increased RR. A lack of synchrony with ventilatory interface and consequent increased RR may have contributed to single patients developing increased hyperinflation and auto-PEEP (42). Furthermore, auto-PEEP is known to lead to decreased venous return and reduced CO (9). A change in stroke volume and/or peripheral resistance could be the mechanism behind the decrease in CI, but the lack of hypotension showed that in any case there were no important clinical consequences. Nevertheless, in AVF the CI is often elevated because of increased oxygen demand by the respiratory muscles and a drop in the CI value sometimes might represent an improvement, whereas an increase in CI might actually mean that the patient is working harder and needing more O_2 delivered (13,14). Since cardiopulmonary interactions during positive pressure ventilation are complex, we cannot exclude the possibility that fluid depletion levels might have influenced CO reduction in some patients.

With regard to pulmonary circulation, at baseline pulmonary hypertension was observed in all the patients, but none of our 19 patients increased pulmonary pressures during NPPV, although in four cases a relevant reduction of PAP occurred.

To our knowledge, this study is the first that evaluates the haemodynamics of NPPV in COPD patients with AVF. Ambrosino *et al.* (43) reported haemodynamics data obtained through invasive methods performed on COPD patients in a clinically stable condition. Ambrosino *et al.* (43) found a significant fall in CO only when an external PEEP of 5 cmH_2O was administered. Nevertheless, patients with AVF due to severe exacerbation of COPD generally have higher auto-PEEP than those in a stable condition (44). Thus, the administration of equal levels of external PEEP may counterbalance or increase auto-PEEP if provided in acute or stable clinical settings (23,42).

We found that Doppler echocardiography is a well-tolerated, efficient evaluation method that can be used at NPPV initiation in acute COPD patients. It is well known that ultrasound examination of the heart is technically difficult in patients with hyperinflation of the lungs (45). However, expert and motivated echocardiograph technicians can obtain suitable images in up to 80–97% of patients (46,47). In our experience, the subcostal approach successfully detected adequate Doppler signals in a large proportion of COPD patients, thus confirming the results of Tramarin *et al.* (48).

In conclusion, our study suggests that the initiation of NPPV is haemodynamically safe for most patients with exacerbated COPD and AVF, although individual COPD patients with AVF may experience reduction in CI in spite of adequate levels of oxygen saturation during initiation of NPPV by facial mask. This event may be associated with patient inability to synchronize with mask ventilation. Consequently, we strongly suggest that particular caution should be used when applying NPPV with predetermined and fixed pressures since a decrease in CO may occur in patients who are hypotensive or have low fluid volume. In addition, to maximize mask ventilation tolerance, attempts to optimize EPAP and IPAP are preferable to scheduled ventilatory support settings. Finally, we recommended Doppler echocardiography as a useful tool for early detection of haemodynamic alterations due to NPPV application in patients with AVF.

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